White
757202

```
=> fil reg;e carboxymethyl cellulose/cn 5
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               0.31       0.46

FILE 'REGISTRY' ENTERED AT 11:37:35 ON 01 NOV 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:   30 OCT 2001  HIGHEST RN 365493-80-7
DICTIONARY FILE UPDATES:  30 OCT 2001  HIGHEST RN 365493-80-7

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER see
HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


E1            1     CARBOXYMETHYL CARUBIN/CN
E2            1     CARBOXYMETHYL CASEIN/CN
E3            2 --> CARBOXYMETHYL CELLULOSE/CN
E4            1     CARBOXYMETHYL CELLULOSE 2-(DIETHYLAMINO)ETHYL P-AMINOBENZOAT
                    E/CN
E5            1     CARBOXYMETHYL CELLULOSE 2-(DIETHYLAMINO)ETHYL P-AMINOBENZOAT
                    E SALT/CN

=> s e3;d ide can;e carboxymethyl amylase/cn 5
L1            2 "CARBOXYMETHYL CELLULOSE"/CN


L1   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2001 ACS
RN   9004-32-4  REGISTRY
CN   Cellulose, carboxymethyl ether, sodium salt (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   12M31XP
CN   1400LC
CN   2000MH
CN   7H3SF
CN   7H3SX
CN   7H4XF
CN   9H4XF
CN   A 0111
CN   A 01H
CN   A 01L
CN   A 01M
CN   A 02SH
CN   A 10M
CN   A 50M
CN   AG Gum
CN   AG Gum HG
CN   AG Gum LV 1
CN   AG Gum LV 2

Searched by: Mary Hale 308-4258 CM-1 12D16
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CN AKU-W 515
CN Akucell 07071
CN Akucell AF 2205
CN Akucell AF 2805
CN Akucell AF 2881
CN Ambergum 1221
CN Ambergum 1521
CN Ambergum 1570
CN Ambergum 3021
CN Ambergum 99-3021
CN AOIH
CN Aquacide I
CN Aquacide II
CN Aqualon 12M31
CN Aqualon 7H
CN Aqualon 7HF
CN Aqualon 7LF-PH
CN Aqualon 7M2
CN Aqualon CMC 12M8
CN Aqualon CMC 7H
CN Aqualon CMC 7H4F
CN Aqualon CMC 7H4XF
CN Aqualon CMC 7HCF
CN Aqualon CMC 7HX
CN Aqualon CMC 7L
CN Aqualon CMC 7LT
CN Aqualon CMC 7M
CN Aqualon CMC 9H4F
CN Aquaplast
CN Aquasorb F-C
CN Aquasorb F-R
CN Aquasorb FC 1/16
CN **Carboxymethyl cellulose**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 12624-09-8, 9045-95-8, 9085-26-1, 54018-17-6, 55607-96-0, 50642-44-9, 37231-14-4, 37231-15-5, 73699-63-5, 80296-93-1, 82197-79-3, 81209-86-1, 117385-93-0, 198084-97-8, 247080-55-3
MF C2 H4 O3 . x Na . x Unspecified
CI COM
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DETHERM*, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLIT, TULSA, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

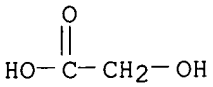
CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 79-14-1
CMF C2 H4 O3

Searched by: Mary Hale 308-4258 CM-1 12D16



17833 REFERENCES IN FILE CA (1967 TO DATE)
607 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17859 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:278027

REFERENCE 2: 135:277998

REFERENCE 3: 135:277780

REFERENCE 4: 135:277218

REFERENCE 5: 135:275028

REFERENCE 6: 135:275027

REFERENCE 7: 135:274878

REFERENCE 8: 135:274612

REFERENCE 9: 135:274400

REFERENCE 10: 135:274298

```
E1            1     CARBOXYMETHYL 4-CHLOROPHENYLDITHIOCARBAMATE/CN
E2            1     CARBOXYMETHYL ACRYLATE/CN
E3            0 --> CARBOXYMETHYL AMYLASE/CN
E4            1     CARBOXYMETHYL AMYLOPECTIN/CN
E5            1     CARBOXYMETHYL AMYLOPECTIN ALUMINUM/CN

=> e hyaluronic acid/cn 5
E1            1     HYALURONATE SYNTHASE PXO1-93 (BACILLUS ANTHRACIS STRAIN STER
                    NE PLASMID PXO1)/CN
E2            1     HYALURONATE SYNTHETASE/CN
E3            1 --> HYALURONIC ACID/CN
E4            1     HYALURONIC ACID .BETA.-PHENYLETHYL ESTER/CN
E5            1     HYALURONIC ACID 2,6-DICHLOROBENZYL ESTER/CN

=> s e3;d ide can;e "chondroitin-6-sulfate"/cn 5
L2            1 "HYALURONIC ACID"/CN


L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   9004-61-9  REGISTRY
CN   Hyaluronic acid (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   ACP
CN   ACP (polysaccharide)
CN   ACP gel
CN   Hyaluronan
CN   Luronit
CN   Mucoitin
```

Searched by: Mary Hale 308-4258 CM-1 12D16

```
CN   Sepracoat
DR   9039-38-7, 37243-73-5, 29382-75-0
MF   Unspecified
CI   PMS, COM, MAN
PCT  Manual registration, Polyester, Polyester formed
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGNL, DRUGU, DRUGUPDATES,
       EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT,
       NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, TOXLIT, USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            7866 REFERENCES IN FILE CA (1967 TO DATE)
             594 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            7876 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  135:278050

REFERENCE   2:  135:278037

REFERENCE   3:  135:278035

REFERENCE   4:  135:277987

REFERENCE   5:  135:277874

REFERENCE   6:  135:271907

REFERENCE   7:  135:271487

REFERENCE   8:  135:271124

REFERENCE   9:  135:270986

REFERENCE  10:  135:270891



E1           1     CHONDROITIN, TETRAKIS(HYDROGEN SULFATE) (ESTER)/CN
E2           1     CHONDROITIN, TRIS(HYDROGEN SULFATE) (ESTER)/CN
E3           0 --> CHONDROITIN-6-SULFATE/CN
E4           1     CHONDROITIN-6-SULFURIC ACID/CN
E5           4     CHONDROITINASE/CN

=> s e4;d ide can;e dermatin sulfate/cn 5
L3           1 "CHONDROITIN-6-SULFURIC ACID"/CN



L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   25322-46-7  REGISTRY
CN   Chondroitin, 6-(hydrogen sulfate) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Chondroitinsulfuric acids, type C (8CI)
OTHER NAMES:
CN   Chondroitin 6-sulfate
CN   Chondroitin C sulfate
CN   Chondroitin sulfate C
CN   Chondroitin sulfate type C

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```

CN Chondroitin sulfuric acid C
CN Chondroitin sulphate C
CN **Chondroitin-6-sulfuric acid**
CN Chondroitinsulfuric acid, type C
DR 9045-60-7, 49718-76-5
MF H2 O4 S . Unspecified
CI COM
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, PROMT, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

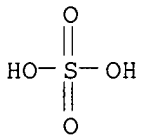
CM 1

CRN 9007-27-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



1789 REFERENCES IN FILE CA (1967 TO DATE)
91 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1791 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:270894

REFERENCE 2: 135:251910

REFERENCE 3: 135:236978

REFERENCE 4: 135:224285

REFERENCE 5: 135:193957

REFERENCE 6: 135:185484

REFERENCE 7: 135:175389

REFERENCE 8: 135:175388

REFERENCE 9: 135:174638

REFERENCE 10: 135:147692

E1 1 DERMATIN (POLYSACCHARIDE)/CN

Searched by: Mary Hale 308-4258 CM-1 12D16

```
E2            1     DERMATIN (STEROID)/CN
E3            1 --> DERMATIN SULFATE/CN
E4            1     DERMATOL/CN
E5            1     DERMATOLACTONE/CN

=> s e3;d ide can;s (heparin or heparin sulfate)/cn
L4            1 "DERMATIN SULFATE"/CN



L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   169799-18-2  REGISTRY
CN   Dermatin (polysaccharide) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Dermatin
CN   Dermatin sulfate
MF   Unspecified
CI   PMS, MAN
PCT  Manual registration
SR   CA
LC   STN Files:   CA, CAPLUS, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
              20 REFERENCES IN FILE CA (1967 TO DATE)
               5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
              20 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  135:262004

REFERENCE   2:  135:185484

REFERENCE   3:  135:102584

REFERENCE   4:  135:82037

REFERENCE   5:  135:81992

REFERENCE   6:  134:105914

REFERENCE   7:  133:242678

REFERENCE   8:  133:148711

REFERENCE   9:  133:84251

REFERENCE  10:  132:339428



              1 HEPARIN/CN
              1 HEPARIN SULFATE/CN
L5            1 (HEPARIN OR HEPARIN SULFATE)/CN

=> d ide can

L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   9005-49-6  REGISTRY
CN   Heparin (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   .alpha.-Heparin
CN   Bemiparin
CN   Certoparin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```

CN Clexane
CN Clivarin
CN Clivarine
CN CY 216
CN CY 222
CN Dalteparin
CN Enoxaparin
CN Fluxum
CN FR 860
CN Fragmin A
CN Fragmin B
CN Fraxiparin
CN **Heparin sulfate**
CN Heparinic acid
CN KB 101
CN Multiparin
CN Novoheparin
CN OP 386
CN OP 622
CN Pabyrn
CN Parnaparin
CN Parvoparin
CN Reviparin
CN Sandoparin
CN Sublingula
CN Vetren
CN Vitrum AB
DR 9075-96-1, 11078-24-3, 11129-39-8, 104521-37-1, 37324-73-5, 91449-79-5
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
17513 REFERENCES IN FILE CA (1967 TO DATE)
1751 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17544 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:278037

REFERENCE 2: 135:278035

REFERENCE 3: 135:277992

REFERENCE 4: 135:273169

REFERENCE 5: 135:271663

REFERENCE 6: 135:271542

REFERENCE 7: 135:271027

REFERENCE 8: 135:270801

Searched by: Mary Hale 308-4258 CM-1 12D16

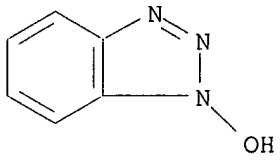
REFERENCE 9: 135:270477

REFERENCE 10: 135:269658

=> e "1-hydroxybenzotriazole hydrate"/cn 5
E1 1 1-HYDROXYBENZOTRIAZOLE/CN
E2 1 1-HYDROXYBENZOTRIAZOLE AMMONIUM SALT/CN
E3 1 --> 1-HYDROXYBENZOTRIAZOLE HYDRATE/CN
E4 1 1-HYDROXYBENZOTRIAZOLE POTASSIUM SALT/CN
E5 1 1-HYDROXYBENZOTRIAZOLE SODIUM SALT/CN

=> s e3;d ide can;e "1-hydroxybenzotriazole monohydrate"/cn 5
L6 1 "1-HYDROXYBENZOTRIAZOLE HYDRATE"/CN

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 80029-43-2 REGISTRY
CN 1H-Benzotriazole, 1-hydroxy-, monohydrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **1-Hydroxybenzotriazole hydrate**
MF C6 H5 N3 O . H2 O
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
CRN (2592-95-2)



● H_2O

13 REFERENCES IN FILE CA (1967 TO DATE)
13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:211059

REFERENCE 2: 135:175350

REFERENCE 3: 135:161827

REFERENCE 4: 135:101931

REFERENCE 5: 134:348237

REFERENCE 6: 134:348236

REFERENCE 7: 133:222965

REFERENCE 8: 131:317743

REFERENCE 9: 127:132746

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 10: 126:144301

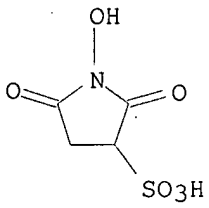
```
E1            1     1-HYDROXYBENZOTRIAZOLE AMMONIUM SALT/CN
E2            1     1-HYDROXYBENZOTRIAZOLE HYDRATE/CN
E3            0 --> 1-HYDROXYBENZOTRIAZOLE MONOHYDRATE/CN
E4            1     1-HYDROXYBENZOTRIAZOLE POTASSIUM SALT/CN
E5            1     1-HYDROXYBENZOTRIAZOLE SODIUM SALT/CN

=> e N-hydroxysulfosuccinimde"/cn 5
MISMATCHED QUOTE IN EXPAND TERM
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> e "N-hydroxysulfosuccinimde"/cn 5
E1            1     N-HYDROXYSUCCINIMIDYL PYRENEBUTANOATE/CN
E2            1     N-HYDROXYSULFONAPHTHALIMIDE/CN
E3            0 --> N-HYDROXYSULFOSUCCINIMDE/CN
E4            1     N-HYDROXYSULFOSUCCINIMIDE/CN
E5            1     N-HYDROXYSULFOSUCCINIMIDE SODIUM SALT/CN

=> s e4;d ide can;e "n-hydroxysuccinimide"/cn 5
L7            1 N-HYDROXYSULFOSUCCINIMIDE/CN
```

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 82436-78-0 REGISTRY
CN 3-Pyrrolidinesulfonic acid, 1-hydroxy-2,5-dioxo- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **N-Hydroxysulfosuccinimide**
CN Sulfo-NHS
FS 3D CONCORD
DR 100839-39-2
MF C4 H5 N O6 S
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, MEDLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

110 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
112 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:238725

REFERENCE 2: 135:179297

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 3: 135:119261

REFERENCE 4: 135:117908

REFERENCE 5: 135:66256

REFERENCE 6: 135:58184

REFERENCE 7: 134:339824

REFERENCE 8: 134:315988

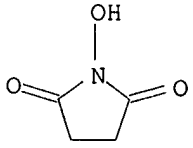
REFERENCE 9: 134:190347

REFERENCE 10: 134:21425

```
E1            1     N-HYDROXYSOLASODINE/CN
E2            1     N-HYDROXYSUCCINAMIC ACID/CN
E3            1 --> N-HYDROXYSUCCINIMIDE/CN
E4            1     N-HYDROXYSUCCINIMIDE 4-AZIDO-2-HYDROXYBENZOATE/CN
E5            1     N-HYDROXYSUCCINIMIDE 4-AZIDOBENZOATE/CN

=> s e3;d ide can;e "4-nitrophenol"/cn 5
L8            1 N-HYDROXYSUCCINIMIDE/CN
```

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 6066-82-6 REGISTRY
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Succinimide, N-hydroxy- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 1-Hydroxy-2,5-pyrrolidinedione
CN 1-Hydroxysuccinimide
CN Hydroxysuccinimide
CN N-Hydroxy-2,5-dioxopyrrolidine
CN **N-Hydroxysuccinimide**
FS 3D CONCORD
MF C4 H5 N O3
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, PIRA, PROMT, SPECINFO, SYNTHLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



Searched by: Mary Hale 308-4258 CM-1 12D16

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2893 REFERENCES IN FILE CA (1967 TO DATE)
171 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2900 REFERENCES IN FILE CAPLUS (1967 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:277895

REFERENCE 2: 135:273466

REFERENCE 3: 135:272864

REFERENCE 4: 135:272741

REFERENCE 5: 135:269657

REFERENCE 6: 135:269619

REFERENCE 7: 135:266385

REFERENCE 8: 135:257454

REFERENCE 9: 135:256981

REFERENCE 10: 135:254069

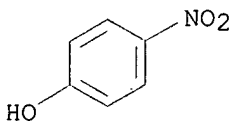
```
E1            1     4-NITROPHENETHYLAMINE HYDROCHLORIDE/CN
E2            1     4-NITROPHENETOLE/CN
E3            1 --> 4-NITROPHENOL/CN
E4            1     4-NITROPHENOL ANION/CN
E5            1     4-NITROPHENOL COMPD. WITH 4-METHYLPYRIDINE (1:1)/CN

=> s e3;d ide can;e "2-nitrophenol"/cn 5
L9            1 4-NITROPHENOL/CN


L9   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   100-02-7  REGISTRY
CN   Phenol, 4-nitro- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Phenol, p-nitro- (8CI)
OTHER NAMES:
CN   1-Hydroxy-4-nitrobenzene
CN   4-Hydroxy-1-nitrobenzene
CN   4-Hydroxynitrobenzene
CN   4-Nitrophenol
CN   Niphen
CN   p-Hydroxynitrobenzene
CN   p-Nitrophenol
FS   3D CONCORD
MF   C6 H5 N O3
CI   COM
LC   STN Files:   AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*,
       DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA,
       MEDLINE, MRCK*, NIOSHTIC, PDLCOM*, PROMT, RTECS*, SPECINFO, SYNTHLINE,
       TOXLIT, ULIDAT, USPATFULL, VETU, VTB
```

Searched by: Mary Hale 308-4258 CM-1 12D16

(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9035 REFERENCES IN FILE CA (1967 TO DATE)
165 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9048 REFERENCES IN FILE CAPLUS (1967 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:278585

REFERENCE 2: 135:278448

REFERENCE 3: 135:273126

REFERENCE 4: 135:273015

REFERENCE 5: 135:272548

REFERENCE 6: 135:266398

REFERENCE 7: 135:266392

REFERENCE 8: 135:266105

REFERENCE 9: 135:264581

REFERENCE 10: 135:261873

```
E1            1     2-NITROPHENETOLE/CN
E2            1     2-NITROPHENIODOXIN-5-IUM CHLORIDE/CN
E3            1 --> 2-NITROPHENOL/CN
E4            1     2-NITROPHENOL ACETATE/CN
E5            1     2-NITROPHENOL CYCLOHEXYLAMINE SALT/CN

=> s e3;e "4-nitrothiophenol"/cn 5
L10           1 2-NITROPHENOL/CN


E1            1     4-NITROTHIOBENZOPHENONE/CN
E2            1     4-NITROTHIOPHENE-2-CARBOXAMIDE/CN
E3            1 --> 4-NITROTHIOPHENOL/CN
E4            1     4-NITROTHIOPHENOL RADICAL ANION/CN
E5            1     4-NITROTHIOPHENOL SODIUM SALT/CN

=> s e3;e "2-nitrothiophenol"/cn 5
L11           1 4-NITROTHIOPHENOL/CN


E1            1     2-NITROTHIOPHENE-4-CARBOXYLIC ACID/CN
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Searched by: Mary Hale 308-4258 CM-1 12D16

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E2            1      2-NITROTHIOPHENE-5-CARBOXALDEHYDE/CN
E3            1 --> 2-NITROTHIOPHENOL/CN
E4            1      2-NITROTHIOPHENOL SODIUM SALT/CN
E5            1      2-NITROTHIOPHENOLATE(1-)/CN

=> s e3;e pentachlorophenol/cn 5
L12           1 2-NITROTHIOPHENOL/CN


E1            1      PENTACHLOROPHENATE SODIUM/CN
E2            1      PENTACHLOROPHENETOLE/CN
E3            1 --> PENTACHLOROPHENOL/CN
E4            1      PENTACHLOROPHENOL .BETA.-D-GLUCOSIDE/CN
E5            1      PENTACHLOROPHENOL .BETA.-GLUCURONIDE/CN

=> s e3;e pentafluoophenol/cn 5
L13           1 PENTACHLOROPHENOL/CN


E1            1      PENTAFLEX 49001/CN
E2            1      PENTAFLIC ACID/CN
E3            0 --> PENTAFLUOOPHENOL/CN
E4            1      PENTAFLUORO(1,2,2,3,3,3-HEXAFLUORO-1-IODOPROPYL)SULFUR/CN
E5            1      PENTAFLUORO(1,2,2-TRIFLUORO-2-METHOXYETHYL)SULFUR/CN

=> e pentafluorophenol/cn 5
E1            1      PENTAFLUOROPERCHLORATOPHOSPHATE(1-)/CN
E2            1      PENTAFLUOROPHENETOLE/CN
E3            1 --> PENTAFLUOROPHENOL/CN
E4            1      PENTAFLUOROPHENOL CATION RADICAL/CN
E5            1      PENTAFLUOROPHENOL ION(1+)/CN

=> s e3;e imidazole/cn 5
L14           1 PENTAFLUOROPHENOL/CN


E1            1      IMIDAZOL-5-YL-METHYLTHIOTETROLIC ACID/CN
E2            1      IMIDAZOLATE/CN
E3            1 --> IMIDAZOLE/CN
E4            1      IMIDAZOLE (ION 1+)/CN
E5            1      IMIDAZOLE 4(OR 5)-CARBOXAMIDE, 5(OR 4)-(N-BENZYLFORMAMIDO)-/
                     CN

=> s e3;e tetrazole/cn 5
L15           1 IMIDAZOLE/CN


E1            1      TETRAZOLAST/CN
E2            1      TETRAZOLAST MEGLUMINE/CN
E3            1 --> TETRAZOLE/CN
E4            1      TETRAZOLE ANION/CN
E5            1      TETRAZOLE CONJUGATE MONOACID/CN

=> s e3;e "4-dimethylaminopyridine"/cn 5
L16           1 TETRAZOLE/CN


E1            1      4-DIMETHYLAMINOPHENYLTROPYLIUM PERCHLORATE/CN
E2            1      4-DIMETHYLAMINOPYRIDAZINE/CN
E3            0 --> 4-DIMETHYLAMINOPYRIDINE/CN
E4            1      4-DIMETHYLAMINOPYRIDINE COMPD. WITH IODINE MONOBROMIDE (1:1)
                     /CN


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```
E5              1     4-DIMETHYLAMINOPYRIDINE COMPD. WITH IODINE MONOCHLORIDE (1:1
                      )/CN

=> s (carbodiimide or "1-ethyl-3-(3-dimethylaminopropyl) carbodiimide" or
"1-ethyl-3-(3-dimethylaminopropyl) carbodiimide")/cn
                1 CARBODIIMIDE/CN
                0 "1-ETHYL-3-(3-DIMETHYLAMINOPROPYL) CARBODIIMIDE"/CN
                0 "1-ETHYL-3-(3-DIMETHYLAMINOPROPYL) CARBODIIMIDE"/CN
L17             1 (CARBODIIMIDE OR "1-ETHYL-3-(3-DIMETHYLAMINOPROPYL) CARBODIIMIDE
                  " OR "1-ETHYL-3-(3-DIMETHYLAMINOPROPYL) CARBODIIMIDE")/CN

=> s (nucleophile or amino acid amide or monofunctional amine or amino acid ester
or amino alcohol or amino thiol or amino phenol or amino catechol or amino acid or
peptide o protein)/cn
                0 NUCLEOPHILE/CN
                0 AMINO ACID AMIDE/CN
                0 MONOFUNCTIONAL AMINE/CN
                0 AMINO ACID ESTER/CN
                0 AMINO ALCOHOL/CN
                0 AMINO THIOL/CN
                0 AMINO PHENOL/CN
                0 AMINO CATECHOL/CN
                0 AMINO ACID/CN
                0 PEPTIDE O PROTEIN/CN
L18             0 (NUCLEOPHILE OR AMINO ACID AMIDE OR MONOFUNCTIONAL AMINE OR
                  AMINO ACID ESTER OR AMINO ALCOHOL OR AMINO THIOL OR AMINO PHENOL
                   OR AMINO CATECHOL OR AMINO ACID OR PEPTIDE O PROTEIN)/CN

=> fil medl,biosis,embase,biotechno,caplus,jicst,wpids
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                              134.70     135.16

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=> s (l1 or l2 or l3 or l4 or l5 or carboxymethyl(w)(cellulose or amylase) or
hyaluronic acid or chondroitin 6(w)(sulfate or sulphate) or dermatin(w)(sulfate or
sulphate) or heparin or heparin(w)(sulfate or sulphate))
L19         61798 FILE MEDLINE
L20         56569 FILE BIOSIS
L21         72925 FILE EMBASE
L22         14104 FILE BIOTECHNO


Searched by: Mary Hale 308-4258 CM-1 12D16
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L23       70348 FILE CAPLUS
L24        8486 FILE JICST-EPLUS
L25       11254 FILE WPIDS

TOTAL FOR ALL FILES
L26      295484 (L1 OR L2 OR L3 OR L4 OR L5 OR CARBOXYMETHYL(W)(CELLULOSE OR
                AMYLASE) OR HYALURONIC ACID OR CHONDROITIN 6(W)(SULFATE OR SULPH
                ATE) OR DERMATIN(W)(SULFATE OR SULPHATE) OR HEPARIN OR HEPARIN(W
                )(SULFATE OR SULPHATE))

=> s l26 and (l6 or l7 or l8 or l9 or l10 or l11 or l12 or l13 or l14 or l15 or l16
or hydroxybenzotriazole(w)(hydrate or monohydrate) or hydroxysulfosuccinimide or
hydroxysuccinimide or nitrophenol or nitrothiophenol or pentachlorophenol or
imidazole or tetrazole or dimethylaminopyridine?)
L27         120 FILE MEDLINE
<------User Break------>
u
SEARCH ENDED BY USER
SEARCH ENDED BY USER

=> s l26 and (l6 or l7 or l8 or l9 or l10 or l11 or l12 or l13 or l14 or l15 or l16
or hydroxybenzotriazole(w)(hydrate or monohydrate) or hydroxysulfosuccinimide or
hydroxysuccinimide or nitrophenol or nitrothiophenol or pentachlorophenol or
imidazole or tetrazole or dimethylaminopyridine?)
L29         120 FILE MEDLINE
L30          59 FILE BIOSIS
L31         107 FILE EMBASE
L32          31 FILE BIOTECHNO
L33         277 FILE CAPLUS
L34           3 FILE JICST-EPLUS
L35          73 FILE WPIDS

TOTAL FOR ALL FILES
L36         670 L26 AND (L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR
                L14 OR L15 OR L16 OR HYDROXYBENZOTRIAZOLE(W)(HYDRATE OR MONOHYDR
                ATE) OR HYDROXYSULFOSUCCINIMIDE OR HYDROXYSUCCINIMIDE OR NITROPH
                ENOL OR NITROTHIOPHENOL OR PENTACHLOROPHENOL OR IMIDAZOLE OR
                TETRAZOLE OR DIMETHYLAMINOPYRIDINE?)

=> s l26 and (l17 or carbodiimide or ethyl(l)dimethylaminopropyl(l)carbodiimide)
L37          59 FILE MEDLINE
L38          75 FILE BIOSIS
L39          65 FILE EMBASE
L40          35 FILE BIOTECHNO
L41         206 FILE CAPLUS
L42           5 FILE JICST-EPLUS
L43          72 FILE WPIDS

TOTAL FOR ALL FILES
L44         517 L26 AND (L17 OR CARBODIIMIDE OR ETHYL(L) DIMETHYLAMINOPROPYL(L)
                CARBODIIMIDE)

=> s l44 and (nucleophile or amino acid amide or monofunctional amine or amino acid
ester or amino alcohol or amino thiol or amino phenol or amino catechol or amino
acid or peptide or protein)
L45          26 FILE MEDLINE
L46          28 FILE BIOSIS
L47          30 FILE EMBASE
L48          18 FILE BIOTECHNO
L49          86 FILE CAPLUS
L50           2 FILE JICST-EPLUS
L51          27 FILE WPIDS

Searched by: Mary Hale 308-4258 CM-1 12D16
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TOTAL FOR ALL FILES
L52 217 L44 AND (NUCLEOPHILE OR AMINO ACID AMIDE OR MONOFUNCTIONAL AMINE OR AMINO ACID ESTER OR AMINO ALCOHOL OR AMINO THIOL OR AMINO PHENOL OR AMINO CATECHOL OR AMINO ACID OR PEPTIDE OR PROTEIN)

=> s l52 and water insolubl?
L53 1 FILE MEDLINE
L54 2 FILE BIOSIS
L55 0 FILE EMBASE
L56 0 FILE BIOTECHNO
L57 6 FILE CAPLUS
L58 0 FILE JICST-EPLUS
L59 3 FILE WPIDS

TOTAL FOR ALL FILES
L60 12 L52 AND WATER INSOLUBL?

=> dup rem l60
PROCESSING COMPLETED FOR L60
L61 9 DUP REM L60 (3 DUPLICATES REMOVED)

=> d cbib abs 1-9

L61 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2001 ACS
2001:45194 Document No. 134:105914 **Water-insoluble** derivatives of polyanionic polysaccharides. Miller, Robert J.; Xu, Xuejian (Genzyme Corporation, USA). U.S. US 6174999 B1 20010116, 10 pp., Cont.-in-part of U.S. Ser. No. 703254. (English). CODEN: USXXAM. APPLICATION: US 1992-833973 19920211. PRIORITY: US 1987-100104 19870918; US 1990-543163 19900625; US 1991-703254 19910520.
AB A **water insol.**, biocompatible compn. that is formed by a method which combines, in an aq. mixt., a polyanionic polysaccharide, a **nucleophile**, and an activating agent, under conditions sufficient to form the compn. Also, a **water insol.**, biocompatible compn. that is formed by a method which combines, in an aq. mixt., a polyanionic polysaccharide, a modifying compd., a **nucleophile** and an activating agent under conditions sufficient to form the compn. Hydrogels were prepd. from sodium hyaluronate, 1-**ethyl**-3-(3-**dimethylaminopropyl**)**carbodiimide** hydrochloride (EDC) as an activating agent, and L-leucine Me ester hydrochloride as a **nucleophile**.

L61 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS
2001:177890 Document No.: PREV200100177890. Method for treating wounds using modified **hyaluronic acid** crosslinked with biscarbodiimide. Kuo, Jing-Wen; Swann, David A.; Prestwich, Glenn D.. ASSIGNEE: Anika Therapeutics, Inc., Woburn, MA, USA; Research Foundation of State University of New York. Patent Info.: US 6096727 August 01, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 1, 2000) Vol. 1237, No. 1, pp. No Pagination. e-file. ISSN: 0098-1133. Language: English.
AB This invention describes a method for preparing **water-insoluble** biocompatible gels, films and sponges by reacting **hyaluronic acid**, or a salt thereof, with a **carbodiimide** in the absence of a **nucleophile** or a polyanionic polysaccharide. The **water-insoluble** gels, films and sponges of this invention may be used as surgical aids to prevent adhesions of body tissues and as drug delivery vehicles.

L61 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS
2000:314509 Document No.: PREV200000314509. **Water-insoluble**

Searched by: Mary Hale 308-4258 CM-1 12D16

derivatives of **hyaluronic acid** and their methods of preparation and use. Kuo, Jing-Wen (1); Swann, David A.; Prestwich, Glenn D.. (1) Stoneham, MA USA. ASSIGNEE: Anika Research, Inc., Woburn, MA, USA; Research Foundation of State University of New York. Patent Info.: US 6013679 January 11, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 11, 2000) Vol. 1230, No. 2, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB This invention describes a method for preparing **water-insoluble** biocompatible gels, films and sponges by reacting **hyaluronic acid**, or a salt thereof, with a **carbodiimide** in the absence of a **nucleophile** or a polyanionic polysaccharide. The **water-insoluble** gels, films and sponges of this invention may be used as surgical aids to prevent adhesions of body tissues and as drug delivery vehicles.

L61 ANSWER 4 OF 9 MEDLINE

2001128095 Document Number: 20556812. PubMed ID: 11103080. Improvement of Schwann cell attachment and proliferation on modified **hyaluronic acid** strands by polylysine. Hu M; Sabelman E E; Tsai C; Tan J; Hentz V R. (Functional Restoration Department, Stanford University, Medical School, Stanford, California, USA.. minhu@hotmail.com) . TISSUE ENGINEERING, (2000 Dec) 6 (6) 585-93. Journal code: C70; 9505538. ISSN: 1076-3279. Pub. country: United States. Language: English.

AB **Hyaluronic acid** (HyA) has the intrinsic ability to promote cell proliferation and reduce scar formation. However, the clinical use of HyA has so far been limited because of its water solubility and nonadhesive characteristics. Increasing interest in HyA as a clinically useful biomaterial has prompted our study of altering HyA's physical properties to render it a potential component of nerve grafts. In this study, strands of HyA were cross-linked by glutaraldehyde (Glut), coated with polylysine, and then inoculated with Schwann cells (SCs). Results in vivo and in vitro demonstrated that cross-linked HyA strands were **water insoluble** and thus less biodegradable. Poly-D-lysine-resurfaced strands showed significant SC attachment of 350-400 cells/mm(2), compared to uncoated controls (0-10 cells/mm(2), $p < 0.01$). Fibroblast control groups showed an attachment of 40-100 cells/mm(2) on coated strands. Immunostaining for proliferating cells showed SCs as and fibroblasts as +. Cells neither adhered to nor proliferated on the modified HyA strands that were not resurfaced. The results suggest that polylysine promotes SC attachment and proliferation to glutaraldehyde-cross-linked HyA strands, the product being a three-dimensional composite with low solubility that may have potential application in nerve grafts.

L61 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1

1994:517825 Document No. 121:117825 **Water-insoluble** derivatives of **hyaluronic acid** and their methods of preparation and use. Kuo, Jing Wen; Swann, David A.; Prestwich, Glenn D. (Anika Research, Inc., USA; Research Foundation of State University of New York). PCT Int. Appl. WO 9402517 A1 19940203, 62 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US7106 19930728. PRIORITY: US 1992-920698 19920728.

AB This invention describes a method for prepg. **water-insol**. biocompatible gels, films and sponges by reacting **hyaluronic acid**, or a salt thereof, with a **carbodiimide** in the absence of a **nucleophile** or a polyanionic polysaccharide. The **water-insol**. gels, films and sponges of this invention may be used as surgical aids to prevent adhesions of body tissues and as drug delivery vehicles. E.g., a deriv. was prepd. from HA and 1-**ethyl**-3-(3-**dimethylaminopropyl**)**carbodiimide**.

Searched by: Mary Hale 308-4258 CM-1 12D16

L61 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2001 ACS
1995:302991 Document No. 122:64475 **Water-insoluble** derivatives of **hyaluronic acid** and their methods of preparation and use. Kuo, Jin-Wen; Swann, David A.; Prestwich, Glenn D. (Research Foundation of State University of N.Y., USA; Anika Research, Inc.). U.S. US 5356883 A 19941018, 13 pp. Cont.-in-part of U.S. Ser. No.809,399, abandoned (English). CODEN: USXXAM. APPLICATION: US 1992-920698 19920728. PRIORITY: US 1989-388578 19890801; US 1991-809399 19911218.

AB This invention describes a method for prepg. **water-insol**. biocompatible gels, films and sponges by reacting **hyaluronic acid** (HA), or a salt thereof, with a **carbodiimide** in the absence of a **nucleophile** or a polyanionic polysaccharide. The **water-insol**. gels, films and sponges may be used as surgical aids to prevent adhesions of body tissues and as drug delivery vehicles. For example, a soln. of HA (5.5 mg/mL; 0.281 mequiv, pH 4.75) was treated with a soln. of 1-**ethyl**-3-(3-**dimethylaminopropyl**)**carbodiimide** (21.46 mg; 0.1097 mmol) and ethanol was added to ppt. the chem. modified HA. When the ppt. was resuspended in water, it formed an insol. gel.

L61 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
1993:87614 Document No. 118:87614 **Water-insoluble** derivatives of polyanionic polysaccharides as surgical adhesion inhibitors and matrixes for sustained-release drugs. Miller, Robert; Burns, James W.; Xu, Xuejian (Genzyme Corp., USA). PCT Int. Appl. WO 9220349 A1 19921126, 46 pp. DESIGNATED STATES: W: AU, CA, FI, JP, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US4212 19920519. PRIORITY: US 1991-703254 19910520; US 1992-833973 19920211.

AB Polyanionic polysaccharides, such as CMC, **hyaluronic acid**, **heparin**, **chondroitin-6-sulfate** and dermatan sulfate, are rendered **water-insol**. by treatment with a **nucleophile**, an activating agent and, optionally, a modifying agent. The **nucleophile** is an **amino acid** or a salt, amide or ester thereof, an **amino alc**., aminothiol, **peptide**, **protein**, etc. The activating agent is 1-**ethyl**-3-(3-**dimethylaminopropyl**)**carbodiimide**-HCl (EDC), a phosphonium hexafluorophosphate, etc. The modifying agent is 1-hydroxybenzotriazole-H2O, N-hydroxysulfosuccinimide, 4-nitrophenol, etc. The products are films, gels or foams, which retain their strength even when hydrated. They are useful for preventing postoperative membrane adhesion or as matrixes for sustained-release drugs. A Na hyaluronate hydrogel was prepd., using EDC as activating agent and leucine Me ester-HCl as **nucleophile**.

L61 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
1989:480259 Document No. 111:80259 **Water-insoluble** biocompatible derivatives of **hyaluronic acid**, their manufacture and use. Hamilton, Raymond G.; Fox, Ellen M.; Acharya, Raksha A.; Watts, Alan E. (Genzyme Corp., USA). PCT Int. Appl. WO 8902445 A1 19890323, 24 pp. DESIGNATED STATES: W: AU, DK, FI, JP, NO; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1988-US2969 19880826. PRIORITY: US 1987-100104 19870918.

AB Gels which can be dewatered or decompd. to give films are prepd. by activating **hyaluronic acid** with an activating agent and derivatizing with a **nucleophile**. The products are useful as agents for controlled release of drugs, as surgical aids, etc. A soln. of Na hyaluronate (400 mg in 40 mL water, adjusted to pH 4.75 with 0.1N HCl) was mixed with 314 mg 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide, followed by 190 mg L-leucine Me ester-HCl to prep. a mixt. (pH 6.2), which

on spreading and drying on a Petri dish surface produced a film insol. in water or 1M aq. NaCl.

L61 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2001 ACS
1984:577555 Document No. 101:177555 Adsorbent for removal of toxic substances from body fluids. Tani, Nobutaka; Hayashi, Tsuneo (Kanegafuchi Chemical Industry Co., Ltd. , Japan). Eur. Pat. Appl. EP 110409 A2 19840613, 39 pp. DESIGNATED STATES: R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1983-112042 19831201. PRIORITY: JP 1982-212379 19821202; JP 1983-31194 19830225; JP 1983-68116 19830418; JP 1983-70967 19830421; JP 1983-187365 19831005.
AB An adsorbent for removing harmful substances from body fluids in extracorporeal circulation comprises a **water-insol.** porous hard gel on which a ligand having an affinity for the substance is immobilized. Thus, Toyopearl HW55 gel was mixed with satd. NaOH aq. soln. and epichlorohydrin and the resulting epoxy-activated gel was further treated with conc. aq. NH3. The resulting amino group-contg. activated gel was treated with **heparin** and further mixed with 1-**ethyl**-3-(**dimethylaminopropyl**)**carbodiimide** while maintaining the reaction mixt. at pH 4.5. The amt. of **heparin** immobilized was 2.2 mg/mL. Removal of low-d. lipoproteins by using the above adsorbent was demonstrated.

=> s l52 and biocompatibl?
L62 8 FILE MEDLINE
L63 3 FILE BIOSIS
L64 1 FILE EMBASE
L65 1 FILE BIOTECHNO
L66 10 FILE CAPLUS
L67 0 FILE JICST-EPLUS
L68 9 FILE WPIDS

TOTAL FOR ALL FILES
L69 32 L52 AND BIOCOMPATIBL?

=> s l169 not l60
<------User Break------>
u
SEARCH ENDED BY USER

=> s l69 not l60
L76 8 FILE MEDLINE
L77 1 FILE BIOSIS
L78 1 FILE EMBASE
L79 1 FILE BIOTECHNO
L80 5 FILE CAPLUS
L81 0 FILE JICST-EPLUS
L82 6 FILE WPIDS

TOTAL FOR ALL FILES
L83 22 L69 NOT L60

=> dup rem l83
PROCESSING COMPLETED FOR L83
L84 16 DUP REM L83 (6 DUPLICATES REMOVED)

=> d 1-16 cbib abs

L84 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2001:101011 Document No. 134:152708 Universal **biocompatible** coating platform for medical devices. Hsu, Li-chien; Hu, Can B.; Tong,

Searched by: Mary Hale 308-4258 CM-1 12D16

Sun-de (Edwards Lifesciences Corporation, USA). PCT Int. Appl. WO 2001008718 A1 20010208, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US20093 20000724. PRIORITY: US 1999-362468 19990728.

AB Universal, **biocompatible** coating platforms for articles intended to contact physiol. fluids or tissues and assocd. methods of prodn. are disclosed. The coating platforms of the present invention are composed of a polyelectrolyte mol. film contg. one or more biol. active compds. The mol. film is further complexed with the surface of an article by a crosslinked interpenetrating network (IPN) made from at least one multifunctional mol. and at least one crosslinking agent. The IPN may entrap addnl. biol. active compds. within the coating platform, or addnl. biol. active compds. may be bound to its outer surface. The coating platform of the present invention is ideally suited for providing medical devices with anti-thrombogenic coatings. A polypropylene hollow fiber oxygenator was coated with a 0.05 % polyethyleneimine (PEI) soln., then followed by a 0.5 % chondroitin sulfate A soln., a mixt. of 0.05 % PEI and 0.5% ethylene glycol diglycidyl ether, and 0.5 % sodium **heparin** soln. to obtain antithrombogenic coating.

L84 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2001 ACS

2001:208136 Document No. 134:242635 Magnetic nanoparticles having biochemical activity, method for the production thereof and their use. Bahr, Michael K.; Berkov, Dimitri; Buske, Norbert; Clement, Joachim; Goernert, Peter; Hoeffken, Klaus; Kliche, Kay-Oliver; Kober, Thomas; Schnabelrauch, Matthias; Vogt, Sebastian; Wagner, Kerstin; Gansau, Christian (Tridelta Bio Medical G.m.b.H., Germany). PCT Int. Appl. WO 2001019405 A2 20010322, 32 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (German). CODEN: PIXXD2. APPLICATION: WO 2000-EP9004 20000914. PRIORITY: DE 1999-19944971 19990914.

AB The invention relates to magnetic nanoparticles, to the prodn. thereof and to their use. The aim of the invention is to prep. nanoparticles which, also in the intracellular area of cells, can specifically bond to intracellular biomacromols. so that a sepn. is made possible by the action of an external magnetic field. This is achieved by using magnetic nanoparticles which have a biochem. activity and which are comprised of a magnetic nuclear particle and of a shell layer that is fixed to the nuclear particle. The nanoparticles contain a compd. of general formula M - S - L - Z (I), whereby the binding sites between S and L and L and Z have covalently bound functional groups. M represents the magnetic nuclear particle, S represents a **biocompatible** substrate fixed to M, L represents a linker grouping, and Z represents a grouping, which is comprised of nucleic acids, **peptides** or **proteins** or of their derivs., and which has at least one structure that is specifically capable of binding with a binding domain of an intracellular biomacromol.

L84 ANSWER 3 OF 16 MEDLINE DUPLICATE 2

2001306450 Document Number: 21153816. PubMed ID: 11255190. In vivo

Searched by: Mary Hale 308-4258 CM-1 12D16

biocompatibility of **carbodiimide**-crosslinked collagen matrices: Effects of crosslink density, **heparin** immobilization, and bFGF loading. van Wachem P B; Plantinga J A; Wissink M J; Beernink R; Poot A A; Engbers G H; Beugeling T; van Aken W G; Feijen J; van Luyn M J. (Laboratory for Tissue Engineering, Medical Biology, University of Groningen, Faculty for Medical Sciences, University Hospital-Entrance 25, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.) JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (2001 Jun 5) 55 (3) 368-78. Journal code: HJJ; 0112726. ISSN: 0021-9304. Pub. country: United States. Language: English.

AB Collagen matrices, crosslinked using N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide (E) and N-hydroxysuccinimide (N), were previously developed as a substrate for endothelial cell seeding of small-diameter vascular grafts. In the present study, the biocompatibility of various EN-crosslinked collagen matrices was evaluated following subcutaneous implantation in rats for periods up to 10 weeks. The effects of the crosslink density, referred to as the number of free primary amino groups per 1,000 **amino acid** residues (EN10, EN14, EN18, or EN22), the amount of **heparin** immobilized to EN14, and the effect of preloading heparinized EN14 with basic fibroblast growth factor (bFGF) on the induced tissue reaction were studied. EN-crosslinked collagen was **biocompatible** at both early and late time intervals, and matrices with high crosslink densities (i.e., EN14, EN10) especially demonstrated a significantly decreased antigenic response when compared to noncrosslinked collagen. Furthermore, increased crosslinking resulted in a decreased degradation rate. Immobilization of **heparin** onto EN14 resulted in a similar to EN14 (thus without **heparin**) or somewhat reduced tissue reaction, but fibrin formation and vascularization were increased with increasing quantities of immobilized **heparin**. Matrices preloaded with bFGF also demonstrated good biocompatibility, especially in combination with higher amounts of immobilized **heparin**. The latter matrices [EN14 with high **heparin** and bFGF, thus EN14-H (0.4)F and EN14-H(1.0)F] demonstrated significantly increased vascularization for periods up to 3 weeks. Neither **heparin** immobilization nor bFGF preloading induced an increased antigenic response. It is concluded that the results of this study justify further evaluation of bFGF preloaded, **heparin** immobilized EN14 collagen, as a matrix for endothelial cell seeding in experimental animals. J Biomed Mater Res 55: 368-378, 2001.

L84 ANSWER 4 OF 16 MEDLINE

2001304564 Document Number: 20550860. PubMed ID: 11101159. Immobilization of **heparin** to EDC/NHS-crosslinked collagen. Characterization and in vitro evaluation. Wissink M J; Beernink R; Pieper J S; Poot A A; Engbers G H; Beugeling T; van Aken W G; Feijen J. (Institute for Biomedical Technology, Department of Chemical Technology, University of Twente, Enschede, The Netherlands.) BIOMATERIALS, (2001 Jan) 22 (2) 151-63. Journal code: A4P; 8100316. ISSN: 0142-9612. Pub. country: ENGLAND: United Kingdom. Language: English.

AB In the present study, **heparin** immobilization to a non-cytotoxic crosslinked collagen substrate for endothelial cell seeding was investigated. Crosslinking of collagen using N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide (EDC) and N-hydroxysuccinimide (NHS) resulted in a material containing 14 free primary amino groups per 1000 **amino acid** residues (E/N14C). At a fixed molar ratio NHS:EDC of 0.6, the amount of **heparin** covalently immobilized to E/N14C increased with increasing molar ratios of EDC to **heparin** carboxylic acid groups (Hep-COOH), to a maximum of approximately 5-5.5 wt% at a ratio of 2. Upon incubation in cell culture medium of endothelial cells, 4 to 7% of the immobilized **heparin** was released during 11 days. Immobilization of increasing amounts of **heparin** to E/N14C progressively reduced activation of contact activation proteases. Optimal

anticoagulant activity, as measured by thrombin inhibition, was obtained after **heparin** immobilization using a ratio of EDC to Hep-COOH of 0.2-0.4 (14-20 mg **heparin** immobilized per gram of collagen). Platelets deposited to (heparinized) E/N14C showed only minor spreading and aggregation, although **heparin** immobilization slightly increased the number of adherent platelets. The results of this study suggest that **heparin** immobilization to EDC/NHS-crosslinked collagen may improve the in vivo blood compatibility of this material.

L84 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
2000:741971 Document No. 133:313688 Lubricious coatings for medical devices. Hsu, Li-Chien; Hu, Can B.; Tong, Sun-De (Edwards Life Sciences Corporation, USA). PCT Int. Appl. WO 2000061205 A1 20001019, 59 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US9344 20000408. PRIORITY: US 1999-290501 19990412.

AB **Biocompatible** surfaces on medical devices, particularly those formed of synthetic materials, are produced by providing coating compds. having crosslinked regions capable of entrapping **biocompatible** mols. on the surfaces of medical devices in order to form a stable base layer. The crosslinked base layer is lubricious and is able to function as an entrapping or coupling site for addnl. **biocompatible** agents, which may be stably incorporated into its crosslinked lattice. Thus, the coatings of the present invention have enhanced lubricity and may also have antimicrobial, **protein**-repelling, and/or antithrombotic properties. Thus, a soln. contained polyethyleneimine 0.3, PVP 0.3, **heparin** complex 0.3, stannous octoate 0.03, and PrOH 300 g. Polyurethane (PU) tubes were first soaked in a 0.2% Denacol 411/GENESOLV soln. for 30 s. After drying, the PU tubes are soaked in the above soln. for 30 s and then dried in a 650.degree. oven for 2 h. Then the tubes were sterilized in ETO. The PU tubes had a pull force of 0.79 lb after a 30-day treatment.

L84 ANSWER 6 OF 16 MEDLINE
2000163394 Document Number: 20163394. PubMed ID: 10701459. Development of tailor-made collagen-glycosaminoglycan matrices: EDC/NHS crosslinking, and ultrastructural aspects. Pieper J S; Hafmans T; Veerkamp J H; van Kuppevelt T H. (Department of Biochemistry, Faculty of Medical Sciences, University of Nijmegen, The Netherlands.) BIOMATERIALS, (2000 Mar) 21 (6) 581-93. Journal code: A4P; 8100316. ISSN: 0142-9612. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The many biocharacteristics of glycosaminoglycans (GAGs) make them valuable molecules to be incorporated in collagenous biomaterials. To prepare tailor-made collagen-GAG matrices with a well-defined biodegradability and (bioavailable) GAG content, the crosslinking conditions have to be controlled. Additionally, the ultrastructural location of GAGs in engineered substrates should resemble that of the application site. Using chondroitin sulfate (CS) as a model GAG, these aspects were evaluated. The methodology was then applied for other GAGs. CS was covalently attached to collagen using 1-ethyl-3-(3-dimethyl aminopropyl) **carbodiimide** (EDC) and N-hydroxysuccinimide (NHS). A maximum of about 155 mg CS/g matrix could be immobilized. CS incorporation and bioavailability, as evaluated by interaction with specific antibodies and glycosidases, was dependent on the molar ratio EDC:carboxylic groups of CS. The denaturation temperature could be modulated from 61 to 85 degrees C. The general applicability of EDC/NHS

for immobilizing GAGs was demonstrated with dermatan sulfate, **heparin**, and heparan sulfate. These matrices revealed comparable physico-chemical characteristics, biodegradabilities, and preserved bioavailable GAG moieties. At the ultrastructural level, GAGs appeared as discrete, electron-dense filaments, each filament representing a single GAG molecule. Distribution was independent of GAG type. They were observed throughout the matrix fibers and at the outer sites, and located, either parallel or orthogonally, at the periphery of individual collagen fibrils. Compositional and ultrastructural similarity between matrices and tissue structures like cartilage and basement membranes can be realized after attachment of specific GAG types. It is concluded that EDC/NHS is generally applicable for attachment of GAGs to collagen. Modulation of crosslinking conditions provides matrices with well-defined GAG contents, and biodegradabilities. Ultrastructural similarities between artificially engineered scaffolds and their possible application site may favor the use of specific collagen-GAG matrices in tissue engineering.

L84 ANSWER 7 OF 16 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-550861 [46] WPIDS
AB WO 9943728 A UPAB: 19991110
NOVELTY - A new polymer (I) consists of a polyurethane (PU) which is covalently bonded to sulfated **hyaluronic acid** (HA) or its derivative.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(i) the preparation of (I);
(ii) hemo-compatible materials (II) comprising or consisting of (I); and
(iii) industrial or medical articles made or coated with (II).

ACTIVITY - Anticoagulant.

MECHANISM OF ACTION - None given.

USE - (I)-based **biocompatible** materials (II) are used for making or coating biomedical articles, and may be in the form of sponges, films, membranes, threads, tampons, non-woven fabrics, microspheres, nanospheres, gauzes, gels and guide channels (all claimed).

Industrial or medical articles made of or coated with (II) are specifically catheters, guide channels, probes, cardiac valves, soft tissue prostheses, prostheses of animal origin such as cardiac valves from pigs, artificial tendons, bone replacements or cardiovascular prostheses, contact lenses, blood oxygenators, artificial kidneys, hearts, pancreas and livers, blood bags, syringes, surgical instruments, filtration systems, laboratory instruments, containers for cultures and for cell and tissue regeneration, or supports for **peptides, proteins** and antibodies (all claimed).

ADVANTAGE - (I) are highly **biocompatible** and hemocompatible. They combine the anticoagulant activity, inhibition of platelet adhesion and resistance to hyaluronidase shown by sulfated HA (or derivatives) with the mechanical properties (resistance to wear, bending etc.) of PU.

Tests on platelet adhesion showed that platelets formed on less than 10% of a coated surface. Tests on blood coagulation gave a coagulation time of over 120 minutes when blood was exposed to (I), compared with 26 minutes for unmodified PU.

(I) are easily applied to polymer surfaces of biomedical objects by dissolving (I) in a solvent which partially dissolves the outer layer of the object.

Dwg.0/4

L84 ANSWER 8 OF 16 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-443873 [37] WPIDS
AB WO 9931167 A UPAB: 19990914
NOVELTY - Preparation of cross-linked, water-swellable polymer particles by combining aqueous solution of water-soluble polymer(s) with functional

group(s) or charge(s) and aqueous medium with oil phase of inert hydrophobic liquid and emulsifier by moderate agitation, etc.

DETAILED DESCRIPTION - Preparation comprises

(1) combining aqueous polymer solution comprising at least one water-soluble polymer with at least one functional group or charge and an aqueous medium with an oil phase comprising an inert hydrophobic liquid and at least one emulsifier under moderate agitation to form an emulsion of droplets of the water-soluble polymer; and

(2) adding to the emulsion at least one cross-linking agent capable of cross-linking the function groups or charges on the water-soluble polymer.

ACTIVITY - Soft-tissue augmentation; tissue growth promotion.

USE - Used in soft-tissue augmentation and to promote tissue growth (claimed). Used for implantation and scaffolding to promote cell growth. Used for medicinal purposes, for treatment of urinary incontinence, vesicouretreral reflux, glottic insufficiency, gastroesophageal reflux or skin defects, and to provide scaffolding material for wound healing and tissue replacement in tissues in the breast, lip, penis, bone, cartilage and tendon. Used for soft-tissue augmentation to treat congenital abnormalities (hemifacial microsmia, malar and zygomatic hypoplasia, unilateral mammary hypoplasia, pectus excavatum, pectoralis agenesis and velopharyngeal incompetence secondary to cleft palate repair and submucous cleft palate), acquired defects (post-surgical, -traumatic and -infectious defects, such as depressed scars, subcutaneous atrophy, acne pitting, linear scleroderma with subcutaneous atrophy, saddle-nose deformity, Romberg's disease and unilateral vocal cord paralysis) or cosmetic defects (glabellar frown lines, nasolabial creases, circumoral geographical wrinkles, sunken cheeks or mammary hypoplasia).

ADVANTAGE - Are **biocompatible**, non-biodegradable, substantially non-cytotoxic, non-carcinogenic, non-inflammatory, non-pyrogenic and non-immunogenic and lack other unwanted humoral or cellular responses. Have sufficient long-term stability of size, shape, rigidity and composition for utility as implant materials. Are relatively inert and do not rapidly degrade in vivo. Are easily injectable.

Dwg.0/0

L84 ANSWER 9 OF 16 MEDLINE

2000001478 Document Number: 20001478. PubMed ID: 10533911.

Surface-immobilized biomolecules on albumin modified porcine pericardium for preventing thrombosis and calcification. Chandy T; Das G S; Wilson R F; Rao G H. (Biomedical Engineering Institute, University of Minnesota, Minneapolis 55455, USA.. chando25@gold.tc.umn.edu) . INTERNATIONAL JOURNAL OF ARTIFICIAL ORGANS, (1999 Aug) 22 (8) 547-58. Journal code: GQO; 7802649. ISSN: 0391-3988. Pub. country: Italy. Language: English.

AB The search for a noncalcifying tissue material to be used for valve replacement application continues to be a field of extensive investigation. A series of porcine pericardial membranes was prepared by modifying the glutaraldehyde--treated tissues with albumin and subsequently immobilizing bioactive molecules like PGE1, PGI2 or **heparin** via the **carbodiimide** functionalities. The in vitro calcification and collagenase degradation of these modified tissues were studied as a function of exposure time. Furthermore, the biocompatibility aspects of such novel interfaces were established by platelet adhesion and fibrinogen adsorption. The results reported in this article propose that the treatment with antiplatelet agents such as albumin, **heparin** and prostaglandins (PGE1 or PGI2) change the surface conditioning of pericardial tissues, suggesting a possible role of deposited serum components in affecting mineralization process on bioprosthesis. Therefore, it is worthy to hypothesize that besides inhibiting the accumulation of calcium in the devitalized cells, the early formation of a conditioning layer on the bioprosthesis surface may affect salt precipitations, determining the propensity of the implant to calcify.

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More detailed studies are needed to understand the involvement of plasma **proteins** and cellular components of the recipient blood in tissue-associated calcification.

L84 ANSWER 10 OF 16 MEDLINE

1998127568 Document Number: 98127568. PubMed ID: 9468054. **Heparin** immobilized on **proteins** usable for arterial prosthesis coating: growth inhibition of smooth-muscle cells. Laemmel E; Penhoat J; Warocquier-Clerout R; Sigot-Luizard M F. (Centre de Recherches, Laboratoire de Biologie Cellulaire Experimentale, Universite de Technologie de Compiegne, France.) JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (1998 Mar 5) 39 (3) 446-52. Journal code: HJJ; 0112726. ISSN: 0021-9304. Pub. country: United States. Language: English.

AB Gelatin or a mixture of albumin and gelatin has been proposed for the coating of vascular grafts according to their surface thrombogenicity and biocompatibility, and the possibility of biodegradation. **Heparin** treatment of hemocompatible surfaces improved the patency of prostheses. In this study, different amounts of **heparin** were immobilized on these **protein** gels using a water-soluble **carbodiimide** [1-**ethyl**-3-(3-**dimethylaminopropyl**) **carbodiimide**]. The results showed a coupling of **heparin** with gelatin and/or albumin at the surface of the gels, stable for as long as 1 month. From 0.20 to 3.60 microg x cm(-2), **heparin** could be immobilized. The antiproliferative activity of immobilized **heparin** was controlled toward bovine smooth-muscle cells grown on these gels. Cell growth inhibition was dose dependent, but the percentages of inhibition were lower at day 8 than at day 4 at any **heparin** concentration used under experimental conditions. Referring to **heparin** in solution, immobilized **heparin** displayed an antiproliferative activity that improved the potential interest for coating.

L84 ANSWER 11 OF 16 MEDLINE

1998193429 Document Number: 98193429. PubMed ID: 9532261. In vitro anti-staphylococcal activity of heparinized biomaterials bonded with combinations of rifampicin. Fallgren C; Utt M; Petersson A C; Ljungh A; Wadstrom T. (Department of Medical Microbiology, University of Lund, Sweden.) ZENTRALBLATT FUR BAKTERIOLOGIE, (1998 Jan) 287 (1-2) 19-31. Journal code: BD7; 9203851. ISSN: 0934-8840. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Biomaterial implants in various human body tissues are highly susceptible to bacterial colonization. We report here on the coating of heparinized biomaterials with **heparin** binding extracellular matrix **proteins** giving special regard to the efficient adsorption and slow release of antibiotics. **Heparin** was partially degraded and the resulting fragments were covalently end-point attached to 0.5 cm long silicone biomaterial surface. Collagen type I was immobilized on the heparinized biomaterials and then cross-linked with acyl-azide or **carbodiimide**. Finally, the resulting biosurfaces were exposed to antibiotics, i.e. rifampicin in combination with cefuroxime, fusidic acid, ofloxacin or vancomycin, respectively. The antibiotic bonded biomaterials were evaluated for their anti-staphylococcal activity after elution in NaCl, serum or blood by measuring the zones of inhibition for S. epidermidis strain RP12. Furthermore, we examined the in-vitro colonization resistance to S. epidermidis RP12 for these combinations of rifampicin-bonded biomaterials by an ATP bioluminescence assay. The ATP measurements showed that initially adherent bacteria were eradicated from the polymer surface, for at least 24 or 48 h (fusidic acid > cefuroxime > vancomycin > ofloxacin). The anti-staphylococcal activity of rifampicin-fusidic acid bonded heparinized biomaterials seems of sufficient duration and efficacy to merit testing in an animal model.

L84 ANSWER 12 OF 16 MEDLINE

Searched by: Mary Hale 308-4258 CM-1 12D16

97328202 Document Number: 97328202. PubMed ID: 9184748. Heparinization of gas plasma-modified polystyrene surfaces and the interactions of these surfaces with **proteins** studied with surface plasmon resonance.
van Delden C J; Lens J P; Kooyman R P; Engbers G H; Feijen J. (University of Twente, Department of Chemical Engineering, Enschede, The Netherlands.) BIOMATERIALS, (1997 Jun) 18 (12) 845-52. Journal code: A4P; 8100316. ISSN: 0142-9612. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Polystyrene surfaces obtained by spin-coating a solution of polystyrene in toluene on a gold layer were functionalized with carboxylic acid groups by preadsorption of the sodium salt of undecylenic acid, followed by an argon plasma treatment. A conjugate of albumin and **heparin** (alb-hep) was covalently immobilized onto the functionalized surface via preactivation of carboxylic acid groups with a water-soluble **carbodiimide**. The immobilization of alb-hep conjugate and the subsequent interactions of the heparinized surface with antithrombin III (ATIII, a **heparin** cofactor) and thrombin were monitored with surface plasmon resonance (SPR). The surface concentration of conjugate as determined with SPR deviated quantitatively from the results obtained with radiolabelled conjugate. The difference in surface concentrations of conjugate obtained with the two methods probably originates from the uncertainty of the refractive index of the alb-hep conjugate in the SPR technique. ATIII could be bound to the surface modified with alb-hep conjugate but not to a polystyrene surface modified with albumin. Rabbit anti-human ATIII did bind to the alb-hep surface previously exposed to ATIII, confirming the presence of surface bound ATIII. The alb-hep immobilized surface was able to bind much more thrombin than ATIII, which is probably due to the less specific **heparin**-thrombin interaction as compared to the **heparin**-ATIII interaction. This study shows that SPR is a technique that can be used to study, in real time, both the modification of polymer surfaces and the subsequent interactions of the modified surfaces with **proteins**.

L84 ANSWER 13 OF 16 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-224081 [29] WPIDS
CR 1999-180035 [15]
AB WO 9515168 A UPAB: 19990416
Compsn. of matter comprises a hyaluronate functionalised with a dihydrazide.

Prepn. of functionalised hyaluronate gels is also claimed.

The dihydrazide is esp. of formula H2N-NH-CO-A-CO-NH-NH2 (I). A = (un)substd. hydrocarbyl or heterohydrocarbyl of 0-20 carbons or heteroatoms (esp. N, O or S).

The compsn. may also comprise at least one additional component (e.g. covalently bonded to an amine gp. of the dihydrazide) such as a fatty acid, topical medicament, perfume, UV absorbing agent, or drug (e.g. an antiinflammatory, antiviral, antifungal or antiproliferative agent.

Functionalised hyaluronate gels may be prepd. by: (a) mixing hyaluronate with a dihydrazide in an aq. soln. to form a hyaluronate-dihydrazide mixt.; (b) adding a **carbodiimide** to the mixt.; and (c) allowing the mixt. to react in the presence of **carbodiimide** under conditions which produce hyaluronate functionalised with dihydrazide.

USE - The compsns. form **biocompatible** gels or hydrogels and can serve as intermediates for attachment of bio-effecting agents, drugs, **peptides**, fluorocarbons, cosmetic agents, oxygen carriers, etc.

The compsns. may be administered to humans or animals, parenterally or topically.

ADVANTAGE - The prepn. of modified **hyaluronic acid** does not compromise the mol. wt. of the HA molecule, can be irreversible or reversible, provides a pendant functional gp. which can act as a versatile coupling site and gives gels with a strength and type which can be easily manipulated.

Searched by: Mary Hale 308-4258 CM-1 12D16

Dwg.0/4
ABEQ US 5616568 A UPAB: 19970512
A composition of matter comprising hyaluronate functionalised with a dihydrazide at glucuronic acid sites of the hyaluronate.
Dwg.0/0
ABEQ US 5652347 A UPAB: 19970909
A method for making a functionalised hyaluronate gel comprising;
(i) mixing hyaluronate with a dihydrazide in a substantially aqueous solution to form a hyaluronate-dihydrazide mixture;
(ii) adding a **carbodiimide** to the hyaluronate-dihydrazide mixture; and
(iii) allowing the hyaluronate-dihydrazide mixture to react in the presence of **carbodiimide** under conditions producing hyaluronate functionalised with dihydrazide.
Dwg.0/4

L84 ANSWER 14 OF 16 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-236814 [29] WPIDS
AB EP 608095 A UPAB: 19940907
Method for attaching a biomolecule having a plurality of carboxyl gps. to an animated solid surface comprises: a) reacting the biomolecule with a **carbodiimide** to effect an activation with the carboxyl gps. of the biomolecule; b) reacting the **carbodiimide**-activated biomolecule with the animated solid surface whereby to covalently bind the biomolecule thereto; and c) either selectively restoring carboxyl gp. functionality lost during step (a) to the surface-bound biomolecule, or removing N-acyl urea gps. from the covalently bound biomolecule.
The **carbodiimide** is a cpd. of formula (I): R1N=C=NR2 (I), R1 = alkyl or cycloalkyl, R2 = alkylaminoalkyl or heterocycloiminoalkyl.
USE/ADVANTAGE - The method can be used to provide devices with **biocompatible** surfaces, including vascular graft tubing, dialysis tubing or membrane, blood oxygenator tubing or membrane, ultrafiltration membrane, intra aortic balloon, blood bag, catheter, suture, soft or hard tissue prosthesis, synthetic prosthesis, artificial organs, and lenses for the eye, such as contact and intraocular lenses. The selective restoration of carboxyl gps. can be carried out by mild hydrolysis and restores the functionality of the biomolecule. The method is ''selective'' since the bonds between the biomolecule and the animated solid surface remain intact.
Dwg.0/0
ABEQ US 5350800 A UPAB: 19941115
Process for enhancing the bioactivity of solid **biocompatible** material contg. free NH2 gps. (e.g. polymers with amino-substd. monomer units) comprises condensn. of a bio-molecule contg. free COOH gps. with a **carbodiimide**, pref. 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide; then condensn. of the adduct with a bio-molecule contg. free COOH gps., e.g. a growth factor, antimicrobial agent, antithrombogenic agent or cell attachment **protein**; and mild hydrolysis with aq. alkali at pH 8-11 and about 0-70 deg.C for at least 1 hr. to cleave excess diimide gps. and restore the bio-molecule activity.
USE/ADVANTAGE - The process provides a means of activating immobilised bioactive molecules which are kept in contact with the body or a body fluid. The process is applicable to immobilising **heparin** or fibronectin on medical devices, synthetic implants, etc., in order to inhibit fibrin deposition on the surfaces and thrombosis, etc.
Dwg.0/0

L84 ANSWER 15 OF 16 MEDLINE
85133135 Document Number: 85133135. PubMed ID: 3973461. Catalytic activity and platelet reactivity of **heparin** covalently bonded to surfaces. Lindon J N; Salzman E W; Merrill E W; Dincer A K; Labarre D; Bauer K A; Rosenberg R R. JOURNAL OF LABORATORY AND CLINICAL MEDICINE,

Searched by: Mary Hale 308-4258 CM-1 12D16

(1985 Feb) 105 (2) 219-26. Journal code: IVR; 0375375. ISSN: 0022-2143. Pub. country: United States. Language: English.

AB **Heparin** was covalently bound to solid substrate surfaces by means of four different chemistries. It was coupled to polymethylacrylate (PMA) beads with glutaraldehyde, **carbodiimide**, or radical polymerization initiated by Ce4+, or to agarose beads with cyanogen bromide. Each of these chemistries produced measurable amounts of surface-bound **heparin**, which was minimally elutable in contact with plasma. Antithrombin (AT) binding by heparinized PMA materials (compared with PMA control beads) ranged from no AT binding for the material heparinized with **carbodiimide** (PMA-Alb-Hep(EDC] to 3.6 micrograms/ml packed beads for the material heparinized by radical polymerization (PMA-MA-Hep). **Heparin**-like catalytic activity of these materials (assayed by measuring the generation of thrombin-antithrombin complex in plasma) correlated well with the amount of **heparin** bound, but not as well with AT binding capacity. Heparinized agarose, which exhibited a large AT binding capacity (2.2 mg AT per milliliter of packed gel), had virtually no catalytic activity because of its inability to release thrombin-antithrombin complex from the surface. Platelet interaction with heparinized materials that exhibit high AT binding capacity was reduced by pretreatment with normal plasma but not by pretreatment with AT-depleted plasma. Platelet interaction with heparinized materials with low AT binding capacities was not reduced by pretreatment with normal plasma. We conclude that AT binding by **heparin** reduces the platelet reactivity of heparinized surfaces.

L84 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2001 ACS

1980:600126 Document No. 93:200126 Enzyme modification by **biocompatible** polymers. Comparative study of trypsin derivatives covalently bound with water-soluble CM-cellulose. Kinstlers, O.; Zagats, R. A.; Torchilin, V. P. (Inst. Org. Synth., Riga, USSR). Bioorg. Khim., 6(9), 1396-403 (Russian) 1980. CODEN: BIKHD7.

AB Trypsin was covalently bound to CM-cellulose, using **carbodiimide** or an azide deriv. of CM-cellulose, to form water-sol. immobilized trypsins. With **carbodiimide**, the highest yield of **protein** binding was obtained when trypsin and CM-cellulose were incubated at low ionic strength before **carbodiimide** addn. The apparent Km values for N.alpha.-benzoyl-L-arginine Et ester hydrolysis by the water-sol. immobilized prepns. did not differ significantly from each other and were 1.5-2-fold greater than the Km for native enzyme. The immobilized trypsin prepns. were significantly more stable to thermal denaturation at 37.degree.and pH 7.4, the prepn. obtained by the azide method being the most stable. On interaction with pancreatic trypsin inhibitor, the immobilized prepns. showed decreased Ki values compared to native enzyme; this may be due to the neg. charge of CM-cellulose, which contributes to increasing the effective inhibitor concn. Lysis of a model fibrin clot by an immobilized trypsin prepn was only 2-fold slower than with native trypsin and the time for complete lysis was increased no more than 2-fold. Thus, the water-sol. immobilized trypsin prepns. maintained the ability to interact with sol. or insol high-mol.-wt. as well as low-mol.-wt. substrates.

=> s (gel or fibre or fibre or membrane or foam)

L85	810419	FILE MEDLINE
L86	979441	FILE BIOSIS
L87	609204	FILE EMBASE
L88	211516	FILE BIOTECHNO
L89	1065529	FILE CAPLUS
L90	288120	FILE JICST-EPLUS
L91	626984	FILE WPIDS

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TOTAL FOR ALL FILES
L92 4591213 (GEL OR FIBRE OR FIBRE OR MEMBRANE OR FOAM)

=> s (drug or protein or biopolymer or synthetic polymer)(1)dispers?
L93 5746 FILE MEDLINE
L94 7718 FILE BIOSIS
L95 5838 FILE EMBASE
L96 2113 FILE BIOTECHNO
L97 14522 FILE CAPLUS
L98 2468 FILE JICST-EPLUS
L99 5809 FILE WPIDS

TOTAL FOR ALL FILES
L100 44214 (DRUG OR PROTEIN OR BIOPOLYMER OR SYNTHETIC POLYMER)(L) DISPERS?

=> s (126 or polyanionic polysaccharide or polysaccharide) and 110 and 1100
L101 0 FILE MEDLINE
L102 0 FILE BIOSIS
L103 0 FILE EMBASE
L104 0 FILE BIOTECHNO
L105 0 FILE CAPLUS
L106 0 FILE JICST-EPLUS
L107 0 FILE WPIDS

TOTAL FOR ALL FILES
L108 0 (L26 OR POLYANIONIC POLYSACCHARIDE OR POLYSACCHARIDE) AND L10
AND L100

=> s (126 or polyanionic polysaccharide or polysaccharide) and 192 and 1100
L109 38 FILE MEDLINE
L110 47 FILE BIOSIS
L111 37 FILE EMBASE
L112 14 FILE BIOTECHNO
L113 158 FILE CAPLUS
L114 60 FILE JICST-EPLUS
L115 191 FILE WPIDS

TOTAL FOR ALL FILES
L116 545 (L26 OR POLYANIONIC POLYSACCHARIDE OR POLYSACCHARIDE) AND L92
AND L100

=> s 1116 and (nucleophile or amino acid amide or monofunctional amine or amino acid ester or amino alcohol or amino thiol or amino phenol or amino catechol or amino acid or peptide or protein)
L117 31 FILE MEDLINE
L118 41 FILE BIOSIS
L119 30 FILE EMBASE
L120 12 FILE BIOTECHNO
L121 103 FILE CAPLUS
L122 47 FILE JICST-EPLUS
L123 130 FILE WPIDS

TOTAL FOR ALL FILES
L124 394 L116 AND (NUCLEOPHILE OR AMINO ACID AMIDE OR MONOFUNCTIONAL
AMINE OR AMINO ACID ESTER OR AMINO ALCOHOL OR AMINO THIOL OR
AMINO PHENOL OR AMINO CATECHOL OR AMINO ACID OR PEPTIDE OR PROTE
IN)

=> s 1124 and (16 or 17 or 18 or 19 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or hydroxybenzotriazole(w)(hydrate or monohydrate) or hydroxysulfosuccinimide or hydroxysuccinimide or nitrophenol or nitrothiophenol or pentachlorophenol or imidazole or tetrazole or dimethylaminopyridine?)

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L125          0 FILE MEDLINE
L126          0 FILE BIOSIS
L127          0 FILE EMBASE
L128          0 FILE BIOTECHNO
L129          1 FILE CAPLUS
L130          0 FILE JICST-EPLUS
L131          1 FILE WPIDS

TOTAL FOR ALL FILES
L132          2 L124 AND (L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR
                L14 OR L15 OR L16 OR HYDROXYBENZOTRIAZOLE(W)(HYDRATE OR MONOHYDR
                ATE) OR HYDROXYSULFOSUCCINIMIDE OR HYDROXYSUCCINIMIDE OR NITROPH
                ENOL OR NITROTHIOPHENOL OR PENTACHLOROPHENOL OR IMIDAZOLE OR
                TETRAZOLE OR DIMETHYLAMINOPYRIDINE?)

<------User Break------>
u
=> s l132 and (l17 or carbodiimide or ethyl(l)dimethylaminopropyl(l)carbodiimide)
L133          0 FILE MEDLINE
L134          0 FILE BIOSIS
L135          0 FILE EMBASE
L136          0 FILE BIOTECHNO
L137          1 FILE CAPLUS
L138          0 FILE JICST-EPLUS
L139          0 FILE WPIDS

TOTAL FOR ALL FILES
L140          1 L132 AND (L17 OR CARBODIIMIDE OR ETHYL(L) DIMETHYLAMINOPROPYL(L)
                 CARBODIIMIDE)

=> d cbib abs;s miller, r?/au,in or miller r?/au,in

L140 ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2001 ACS
1991:488793   Document No. 115:88793  Method for immobilization of biologically
     active substances on carrier for affinity purification or other purposes.
     Tanihara, Masao; Oka, Kiichiro; Watanabe, Mari; Nakaji, Shuhei (Kuraray
     Co., Ltd., Japan).  Jpn. Kokai Tokkyo Koho JP 03032740 A2 19910213 Heisei,
     8 pp.  (Japanese).  CODEN: JKXXAF.  APPLICATION: JP 1989-170029 19890630.
AB   Biol. active substances (e.g. nucleic acid, protein, lipid) can
     be immobilized by covalently bonding the biol. active substance on an
     active group-contg. carrier [e.g. cellulose, poly(vinyl alc.),
     polyacrylamide, agarose, porous glass, etc.], contacting the biol. active
     substance-contg. carrier with a blocking agent (e.g. glycine,
     ethanolamine, Tris), and then washing the carrier with pH <3.5 buffer and
     pH >5.5 buffer alternately.  The obtained immobilized biol. active
     substance can be used in affinity purifn. of biol. substances of interest
     or in medical treatment (e.g. removal of causative factor from the blood
     of autoimmune disease patients).  Thus, CM-cellulose particles were
     suspended in dioxane; N-hydroxysuccinimide (or dicyclohexyl
     carbodiimide) was added in the suspension with shaking for mixing;
     the mixt. was washed with MeOH and dioxane to obtain a dioxane-contg.
     gel; the gel was then dispersed in a
     NaCl-contg. pH 7.4 phosphate buffer to obtain a carrier for
     immobilization.  A mouse IgG1 monoclonal antibody was then mixed with the
     carrier to obtain an immobilized antibody-contg. gel.  The
     antibody-contg. gel was then washed with a pH 7.4 phosphate
     buffer contg. glycine and NaCl for blocking.  The resulting gel
     was then washed with a pH 2.5 phosphate buffer contg. 100 mM glycine and a
     pH 7.4 phosphate buffer contg. 150 mM NaCl alternately for 6 times.
     Immunoassay demonstrated the binding of the antibody on the gel
     was better than that by a conventional method.


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'IN' IS NOT A VALID FIELD CODE
L141 6270 FILE MEDLINE
L142 8584 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L143 4906 FILE EMBASE
'IN' IS NOT A VALID FIELD CODE
L144 885 FILE BIOTECHNO
L145 7476 FILE CAPLUS
L146 58 FILE JICST-EPLUS
L147 1485 FILE WPIDS

TOTAL FOR ALL FILES
L148 29664 MILLER, R?/AU,IN OR MILLER R?/AU,IN

=> s xu, x?/au,in or xu x?/au,in
'IN' IS NOT A VALID FIELD CODE
L149 1499 FILE MEDLINE
L150 2582 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L151 1351 FILE EMBASE
'IN' IS NOT A VALID FIELD CODE
L152 536 FILE BIOTECHNO
L153 6824 FILE CAPLUS
L154 208 FILE JICST-EPLUS
L155 492 FILE WPIDS

TOTAL FOR ALL FILES
L156 13492 XU, X?/AU,IN OR XU X?/AU,IN

=> s l148 and l156
L157 2 FILE MEDLINE
L158 4 FILE BIOSIS
L159 2 FILE EMBASE
L160 2 FILE BIOTECHNO
L161 4 FILE CAPLUS
L162 0 FILE JICST-EPLUS
L163 1 FILE WPIDS

TOTAL FOR ALL FILES
L164 15 L148 AND L156

=> dup rem l164
PROCESSING COMPLETED FOR L164
L165 5 DUP REM L164 (10 DUPLICATES REMOVED)

=> d 1-5 cbib abs

L165 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
2001:340533 Document No.: PREV200100340533. Water insoluble derivatives of polyanionic polysaccharides. **Miller, Robert J. (1); Xu, Xuejian.** (1) E. Sandwich, MA USA. ASSIGNEE: Genzyme Corporation. Patent Info.: US 6174999 January 16, 2001. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 16, 2001) Vol. 1242, No. 3, pp. No Pagination. e-file. ISSN: 0098-1133. Language: English.
AB A water insoluble, biocompatible composition that is formed by a method which combines, in an aqueous mixture, a polyanionic polysaccharide, a nucleophile, and an activating agent, under conditions sufficient to form the composition. Also, a water insoluble, biocompatible composition that is formed by a method which combines, in an aqueous mixture, a polyanionic polysaccharide, a modifying compound, a nucleophile and an activating

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agent under conditions sufficient to form the composition.

L165 ANSWER 2 OF 5 MEDLINE DUPLICATE 2
1998016241 Document Number: 98016241. PubMed ID: 9351905. Metabolic profiles of montelukast sodium (Singulair), a potent cysteinyl leukotriene1 receptor antagonist, in human plasma and bile. Balani S K; **Xu X**; Pratha V; Koss M A; Amin R D; Dufresne C; **Miller R R** ; Arison B H; Doss G A; Chiba M; Freeman A; Holland S D; Schwartz J I; Lasseter K C; Gertz B J; Isenberg J I; Rogers J D; Lin J H; Baillie T A. (Department of Drug Metabolism, Merck Research Laboratories;.) DRUG METABOLISM AND DISPOSITION, (1997 Nov) 25 (11) 1282-7. Journal code: EBR; 9421550. ISSN: 0090-9556. Pub. country: United States. Language: English.

AB Montelukast sodium [1- [(1(R)-(3-(2-(7-chloro-2-quinolinyl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl)thio]meth yl cyclopropylacetic acid sodium salt] (MK-476, Singulair) is a potent and selective antagonist of the cysteinyl leukotriene (Cys-LT1) receptor and is under investigation for the treatment of bronchial asthma. To assess the metabolism and excretion of montelukast, six healthy subjects received single oral doses of 102 mg of [14C]montelukast, and the urine and feces were collected. Most of the radioactivity was recovered in feces, with </=0.2% appearing in urine. Based on these results and the reported modestly high oral bioavailability of montelukast, it could be concluded that a major part of the radioactivity was excreted via bile. A second clinical study was conducted to identify biliary metabolites of montelukast. The bile was aspirated using a modified procedure involving a nasogastric tube placed fluoroscopically near the ampulla of Vater, after an oral dose of 54.8 mg of [14C]montelukast. This technique appears to be a new application for drug metabolism studies. The study was conducted with fasted and nonfasted subjects, with the bile being aspirated continuously under suction over periods of 2-8 hr and 8-12 hr after the dose, respectively. Two hours before the end of the collection procedure, cholecystokinin carboxyl-terminal octapeptide was administered iv to stimulate gallbladder contraction. Plasma samples also were collected periodically over 10 hr. Due to the nature of the collection procedure and the limited sampling time, recovery of radioactivity in bile was incomplete and varied from 3 to 20% of the dose. Radiochromatographic and LC-MS/MS analyses of bile showed the presence of one major and several minor metabolites, along with small amounts of unchanged parent drug. The minor metabolites were identified, by LC-MS/MS comparison with synthetic standards or by NMR, as acyl glucuronide (M1), sulfoxide (M2), 25-hydroxy (a phenol, M3), 21-hydroxy (diastereomers of a benzylic alcohol, M5a and M5b), and 36-hydroxy (diastereomers of a methyl alcohol, M6a and M6b) analogs of montelukast. The major metabolite was characterized as a dicarboxylic acid (M4), a product of further oxidation of the hydroxymethyl metabolite M6. Chiral LC-MS/MS analyses of M4 revealed that this diacid, like M5 and M6, was formed in both diastereomeric forms. The levels of metabolites in the systemic circulation were low in the fed as well as fasted subjects, with <2% of the circulating radioactivity being due to metabolites M5a, M5b, M6a, and M6b. Overall, this bile aspiration technique, which is less invasive than either T-tube drainage or fine-needle percutaneous puncture, provided a convenient and expedient means of identifying the biliary metabolites of montelukast, relatively free of contributions from colonic microflora.

L165 ANSWER 3 OF 5 MEDLINE DUPLICATE 3
96094304 Document Number: 96094304. PubMed ID: 7493943. Differential regulation of Ca2+ release-activated Ca2+ influx by heterotrimeric G proteins. **Xu X**; Kitamura K; Lau K S; Muallem S; **Miller R T**. (Department of Physiology, University of Texas Southwestern Medical Center, Dallas 75235, USA.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Dec 8) 270 (49) 29169-75. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

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AB The least understood aspect of the agonist-induced Ca2+ signal is the activation and regulation of the Ca2+ release-activated Ca2+ influx (CRAC) across the plasma membrane. To explore the possible role of heterotrimeric G proteins in the various regulatory mechanisms of CRAC, continuous renal epithelial cell lines stably expressing alpha 13 and the constitutively active alpha qQ209L were isolated and used to measure CRAC activity by the Mn2+ quench technique. Release of intracellular Ca2+ by agonist stimulation or thapsigargin was required for activation of CRAC in all cells. Although the size of the internal stores was similar in all cells, CRAC was 2-3-fold higher in alpha 13- and alpha qQ209L-expressing cells. However, the channel was differentially regulated in the two cell types. Incubation at low [Ca2+]i, inhibition of the NOS pathway, or inhibition of tyrosine kinase inhibited CRAC activity in alpha 13 but not alpha qQ209L cells. Treatment with okadaic acid prevented inhibition of the channel by low [Ca2+]i and the protein kinase inhibitors in alpha 13 cells. These results suggest that expression of alpha qQ209L dominantly activates CRAC by stabilizing a phosphorylated state, whereas expression of alpha 13 makes CRAC activation completely dependent on phosphorylation by several kinases. G proteins may also modulate CRAC activity independently of the phosphorylation/dephosphorylation state of the pathway to increase maximal CRAC activity. Furthermore, our results suggest a general mechanism for regulation of CRAC that depends on coupling of receptors to specific G proteins.

L165 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2001 BIOSIS
1996:3920 Document No.: PREV199698576055. The physiological disposition and metabolism of MK-0476 in rats and rhesus monkeys. **Xu, Xin (1)**; **Miller, R.**; Tocco, D.; Wong, B.; Lin, J. H.. (1) Dep. Drug Metab., Merck Res. Lab., West Point, PA 19486 USA. Pharmaceutical Research (New York), (1995) Vol. 12, No. 9 SUPPL., pp. S344. Meeting Info.: Annual Meeting of the American Association of Pharmaceutical Scientists Miami Beach, Florida, USA November 5-9, 1995 ISSN: 0724-8741. Language: English.

L165 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
1993:87614 Document No. 118:87614 Water-insoluble derivatives of polyanionic polysaccharides as surgical adhesion inhibitors and matrixes for sustained-release drugs. **Miller, Robert**; Burns, James W.; Xu, Xuejian (Genzyme Corp., USA). PCT Int. Appl. WO 9220349 A1 19921126, 46 pp. DESIGNATED STATES: W: AU, CA, FI, JP, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US4212 19920519. PRIORITY: US 1991-703254 19910520; US 1992-833973 19920211.

AB Polyanionic polysaccharides, such as CMC, hyaluronic acid, heparin, chondroitin-6-sulfate and dermatan sulfate, are rendered water-insol. by treatment with a nucleophile, an activating agent and, optionally, a modifying agent. The nucleophile is an amino acid or a salt, amide or ester thereof, an amino alc., aminothiol, peptide, protein, etc. The activating agent is 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide-HCl (EDC), a phosphonium hexafluorophosphate, etc. The modifying agent is 1-hydroxybenzotriazole-H2O, N-hydroxysulfosuccinimide, 4-nitrophenol, etc. The products are films, gels or foams, which retain their strength even when hydrated. They are useful for preventing postoperative membrane adhesion or as matrixes for sustained-release drugs. A Na hyaluronate hydrogel was prepd., using EDC as activating agent and leucine Me ester-HCl as nucleophile.

=> log y

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FULL ESTIMATED COST	274.36	409.52

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